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### ► **To cite this version:**

Olivier Lavaine, Julie Spizzo, Claire Arbitre, Jason Muller, Pierre Kuhn, et al.. COVID-19 in children at Strasbourg University Hospital: A retrospective study of the first 2 months of the epidemic. Archives de Pédiatrie, 2021, 28 (5), pp.405-410. <10.1016/j.arcped.2021.03.013>. <hal-03352485>

**HAL Id: hal-03352485**

**<https://hal.science/hal-03352485v1>**

Submitted on 13 Jun 2023

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# **COVID-19 in children at Strasbourg University Hospital: A retrospective study of the first 2 months of the epidemic**

Short title: COVID-19 in children at Strasbourg University Hospital

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**Conflicts of interest:** none

## Summary

*Context:* The emergence and rapid spread of coronavirus disease 2019 (COVID-19) have shaken the planet, both in terms of health and economical aspects, constituting a real challenge for the scientific community.

*Problem:* At the time of the arrival of the epidemic in France, there were limited data regarding how COVID-19 could affect children. A lesser severity compared with adults was described, but knowledge concerning clinical forms and screening strategies was missing.

*Methodology:* In this retrospective and non-interventional epidemiological study, we aimed to describe the epidemiology and the clinical features of COVID-19 pediatric disease in the first university hospital affected by the epidemic in France. We included all underage patients who tested positive for SARS-CoV-2 by polymerase chain reaction (PCR) assays on nasopharyngeal smears performed between February 25, 2020 and April 30, 2020.

*Results:* The presence of fever and respiratory signs was frequent (> 50%), as was the presence of general or digestive signs, but patients were also frequently asymptomatic, making the discovery of a positive smear fortuitous. There were no deaths in our cohort.

*Conclusion:* No patient with a serious form of COVID-19 was treated in the pediatrics departments of Strasbourg University Hospital during the first 2 months of the epidemic. Diagnostic strategies have evolved over the course of the epidemic, ranging from exploring relevant symptoms to systematic screening.

**Keywords:** COVID-19 - pandemic – pediatrics – epidemiology – diagnosis – screening

## **1. Introduction**

The SARS-CoV-2 virus, which appeared in the city of Wuhan, China in late 2019, quickly spread around the world, causing a severe pandemic.

Just over 4 months after its emergence in mid-May 2020, more than 4 million confirmed cases were reported worldwide, with nearly 300,000 deaths [1]. France has not been spared, with a heavy toll of more than 140,000 confirmed cases and nearly 27,000 deaths during that time.

Among the first French clusters identified, the departments of the Haut-Rhin and then the Bas-Rhin were hit with full force, overwhelming in a few days the intensive care and resuscitation units. Also on the frontline, the activity of adult emergency services was completely shaken, with an influx of COVID-positive patients in more than 80% of cases and in a hospitalization rate above 50%.

Against this background, we also prepared ourselves, in the pediatric departments, for the arrival of COVID patients, adjusting both the management of the cases and the number of caregivers available. However, we finally witnessed a "paradoxical" effect of the epidemic, with a drop in the pediatric emergency activity to 25% of its annual average and a clear change in the usual reasons for consultation. Better yet, we had only one patient with COVID-19 confirmed requiring resuscitation care. However, a significant number of screenings were carried out on children, with sometimes very unexpected circumstances of discovery of SARS-CoV-2.

Because they constitute a large proportion of our population, with more than 15 million minors [2] including 12,875,650 students [3], understanding the epidemic in children was essential in order to adapt our medical care but also to manage strategies for confining a population whose potential of contagiousness is not negligible: number of asymptomatic carriers, difficulties in applying the recommendations such as wearing a mask, frequent hand washing, barrier measures.

Thus, in the course of the development of local and national management recommendations, and considering new data suggesting significant clinical heterogeneity and less severity in children [4], we decided to conduct a retrospective descriptive epidemiological study on COVID-positive patients under the age of 18 years at Strasbourg University Hospital (SUH).

The main objective was to describe the epidemiology of children infected by the virus (identified in this article as COVID+) in the first university hospital affected by the epidemic in France. The secondary objectives were to identify the various clinical presentations and to describe the particular circumstances that led to the diagnosis.

## **2. Material and Methods**

The study was a descriptive, retrospective, single-center and non-interventional epidemiological study, based on medical records, covering the period from February 25, to April 30, 2020.

The first pediatric sample for SARS-CoV-2 in our hospital was realized on 25/02/2020 and the first test date with positive results was on February 29, 2020. We decided to limit our study to 2 months arbitrarily, but with the aim of covering the first epidemic wave of COVID-19 in Alsace and being able, at the same time, to draw information from it quickly enough to share it with our colleagues and relate our experience in pediatric services.

Any minor patient who had a positive SRAS-CoV-2 PCR-RT result after sampling at SUH was eligible for inclusion in the study.

The exclusion criteria were patients older than 18 years, patients whose sampling by PCR was carried out outside SUH (city laboratory or any other hospital structure), and the absence of a computerized medical file for the patient.

To find all the records of patients who were tested for SARS-CoV-2 and identify those who had a positive result, we contacted the public health department, which extracted and analyzed the data from the virology laboratory and provided us with a list of patients with a positive test result, the consultation and sample collection date and the department in which it took place, and also a weekly monitoring of the number of screenings and positive cases. The data used for the analysis were collected from the local electronic health records. The protocol used for real-time RT-PCR assays was the technique provided by the Institut Pasteur [5] with a sensitivity of approximately 100 copies of RNA genome equivalent per reaction and a specificity close to 100%.

Among the data collected, we took into account the following: the patient's age; date, reason, and place of consultation; justification or reason for taking the sample for SARS-CoV-2; clinical features such as the presence of fever ( $>38^{\circ}\text{C}$ ), value of pulsed oxygen saturation ( $\text{SpO}_2$ ) in ambient air, presence or absence of signs of acute respiratory distress and associated clinical signs (digestive, neurological, cutaneous, etc.); hospitalization with duration and unit if applicable; and, finally, the main diagnosis recorded at the end of the consultation or stay.

Before collecting the data, we sought the advisory opinion of the Ethics Committee, which responded favorably to our request (reference CE-2020-55). Data processing was validated

and recorded in the SUH register under the number 20-029. The families of all the patients whose data were used were contacted by telephone to inform them of the existence of the study and to guarantee their non-opposition to its completion. An information notice and an objection form in the event of a change of opinion were also sent to them by post.

### **3. Results**

Between February 25 and April 30, 2020, in the various departments of the SUH, a total of 11,545 tests for SARS-CoV-2 RT-PCR were made involving 8908 patients, including 628 samples analyzed from 521 children, some being tested several times. In total, 46 patients tested positive (8.5%). Among them, 13 patients had no usable data: 10 children had been tested at the COVID-19 Sampling Center of the SUH without any clinical examination, one newborn had no medical records, and two were finally false-positive results, which allowed us to conduct the study on a total of 33 COVID+ minor patients (**Figure 1**). No family objected to the use of their child's data.

In this cohort of 33 patients, the median age was 1 year and 9 months, with a mean age of 5 years and 5 months. The oldest patient was 17 years and 8 months old at the time of diagnosis, while the youngest patient was 9 days old. The male–female ratio was 0.6.

**Figure 2** shows the number of tests performed per week and a comparison between sampling of adult patients and minor patients. The increase in the number of tests was similar in the two groups between the first screenings of weeks 9 and 10 and the epidemic peak at around weeks 13–14 for adults, weeks 14–17 for minor patients; the number of positive samples per week was relatively stable over the 2 months for pediatric patients, while it was 10-fold higher for adults.

Out of 628 tests carried out on minors, 257 (41%) were taken in the emergency department (ED), including the Short-Term Hospitalization Unit. Overall, 26 COVID+ patients were tested in the ED among the 33 COVID+ (79%): 25 patients in the pediatric ED, and one minor patient in the adult ED.

While the first screenings were made in the isolation unit of the ED or directly in a room of the STHU, the number of potential cases quickly multiplied and the changing perceptions of risk situations modified our practices.

Finally, sampling for PCR took place in almost all pediatric units: 67 samples in the conventional pediatric departments (where, however, among the four positive cases, three corresponded to positivity controls in patients screened in the pediatric ED), neonatology (one patient from 58 tests), the two pediatric surgery units (four positive patients from 30 tests done), and the pediatric onco-hematology unit (one COVID+ sample out of 27 smears).

**Table 1** describes the different clinical presentations and the orientation of COVID+ patients.

The medical reasons for emergency unit visits for patients who subsequently tested positive were varied, with fever and/or respiratory or digestive symptoms in 64% of cases, but also unrelated to the viral infection in 36% of cases: general pediatrics, traumatology, psychiatry, endocrinology, etc. The circumstances that led to the decision to test the COVID+ patients:

- Firstly, patients with COVID-compatible symptomatology (fever and/or rhinitis, cough, dyspnea), which represent 45.4% of the cases ( $n = 15$ ). Among them, four consulted spontaneously, nine were referred to the SUH for sampling because of contact with a proven case at the very beginning of the epidemic, and two due to comorbidities: a patient with end-stage renal disease on dialysis and another suffering from cystic fibrosis.

- Six infants younger than 6 weeks consulted for fever and were tested as part of the systematic assessment for this age (18.2%).
- Twelve patients (36.4%) benefited from testing because of their hospitalization, whether it was scheduled or not: urgent surgical procedures, notably oncological (biopsy, osteosynthesis), antibody cure, adjustment for diabetes, poor weight gain assessment, etc.

In terms of hospitalizations, 26 of the 33 patients in our study were hospitalized, representing a hospitalization rate of 78.8%, with an average length of stay of 5.4 days. Nevertheless, it seems interesting to include in the calculation the 11 patients with a positive test but no medical records, because 10 of them were only tested in an ambulatory setting (since they were asymptomatic or with very few signs), which led to a hospitalization rate of 61.4%.

In addition, we observed that six of the COVID+ children under 6 weeks of age had an average length of stay of 1.3 days.

It should be mentioned that at the very start of the epidemic, two children were hospitalized with their mother who was also COVID+, for a period of 7 days to ensure medical quarantine. One patient (3%) required resuscitation care due to septic shock from a digestive origin.

Among the 33 patients of the study, the main diagnoses recorded were:

- A COVID-19 disease in 54.5% of cases ( $n = 18$ )
- In 18.1% of cases ( $n = 6$ ) linked to a known pathology already followed up in the SUH (treatment of neuroblastoma, idiopathic scoliosis, type 1 diabetes, postoperative wound trimming, etc.)
- Not directly related to COVID-19 in seven patients (21.2%), and corresponded to an emergency situation (metabolic disease, hypophosphatasia, suspicion of Hirschsprung

disease, hypertrophic heart disease, posttraumatic bifemoral fracture, pyloric stenosis, voluntary drug ingestion).

#### **4. Discussion**

The characteristics of the 33 COVID+ patients in our study are similar to those reported in studies previously conducted in the pediatric population [4,6], especially in terms of average age (5 years and 5 months) and the distribution of boys and girls (sex ratio 0.6).

Regarding the clinical expression of the disease, more than half of the COVID+ patients in our cohort had fever and/or respiratory signs, and one third of them presented with general symptoms. Digestive symptoms were also observed in 18.2% of patients and the classic anosmia–ageusia association was found only once, although its interpretation is difficult given the age of the patients affected. Nearly one fifth of our patients who tested positive were completely asymptomatic (21.2%).

There is a similar distribution of symptoms in the Italian cohort of the CONFIDENCE [6] study (100 patients), in the American study Coronavirus Disease 2019 in Children [7] (291 patients), and in the Chinese study (271 patients) conducted by Lu et al. [8].

In our study, the proportion of COVID+ patients who were hospitalized was significant (61.4%), for an average hospital stay of 5.4 days. By comparison, 67 of the 100 patients in the CONFIDENCE study [6] were hospitalized. However, we should consider that from the start of the epidemic, only patients suspected of having COVID-19 with severity criteria (respiratory distress, SpO<sub>2</sub> <94%, fever poorly tolerated, deterioration of general condition) or a serious comorbidity were tested. The future outlook was an important criterion of sampling,

along with admission screening, independently of whether or not the patient had suspected COVID symptoms. Therefore, all ambulatory patients who did not have severity criteria or hospitalization criteria were not systematically tested. This helps us better understand the variations in the hospitalization rate as a function of time, from 0 to 100%, but also its high average value, greater than 60%.

The subgroup of infants under 6 weeks of age who were hospitalized with fever had an average length of stay of 1.3 days, which suggests mild illness, often warranting short hospital surveillance. At this age, if it were not for the current epidemic, a fever would often require more systematic invasive examinations and longer stays.

One child required intensive care, due to septic shock with a digestive pathogen isolated after blood culture. However, it can be considered that the stay was not related to care concerning clinical manifestations of COVID. In the Chinese study by Dong et al. [4], the percentage of patients whose clinical condition was considered severe and critical was 5.8% of the cohort of 2135 patients. However, the late appearance of post-infectious manifestations after our study period showed us that severe forms of COVID-19 exist and requires us to be more cautious. There were seven patients with pediatric inflammatory multisystem syndrome hospitalized in the ICU from April 16 to May 18 at the SUH, a proportion that is not negligible compared with the number of positive patients in the same hospital. A study is currently underway at the SUH.

On March 19, it was decided to create a conventional COVID pediatric hospitalization unit, located in the infants' department, with six individual rooms dedicated to confirmed or highly suspected cases, until the results were obtained, without criteria of age or underlying condition. Two dedicated COVID rooms were also reserved in the pediatric intensive care unit (which did not receive any patients), and three COVID beds were fitted out in the

neonatal department in the case of the birth of babies with a COVID+ mother. With a variable occupancy rate of the conventional unit from 60 to 80%, these adjustments made it possible to hospitalize patients with suspected COVID by reducing the number of caregivers exposed and by limiting intrahospital dissemination. These rooms also permitted us to receive, outside their usual circuit, several children from the surgery department in the post-operative period suspected of having COVID or of having been contaminated by their surroundings.

The diagnostic strategy, and in particular the sampling criteria, evolved in parallel with the epidemic and all the children who had clinical signs compatible with COVID were not tested.

During the emergence phase of the first cases in Alsace, samples were taken from any patient with fever, with respiratory symptoms (cough and/or dyspnea), and a notion of contagion with a confirmed case or of travel to an area at risk in the previous 2 weeks. The first suspected patients were systematically hospitalized and isolated, pending the outcome, and hospitalization was maintained in the event of positivity to limit the risk of spreading the virus in the population. Very quickly, we realized that quarantine in the hospital was a cumbersome and an unmanageable solution due to the increase in the number of suspected cases, and thus the practice evolved toward testing in the hospital, and then a return home while waiting for the results, in the absence of signs of severity. A quarantine of 14 days was recommended for the whole family if the result turned out to be positive.

Because of the sudden and massive expansion of the epidemic, the availability of smears and laboratory analyses was limited, with an average number of 400 tests per day initially despite a higher demand. This resulting in a change in the SARS-CoV-2 screening protocol, limiting the indications for sampling to patients with signs of severity and requiring hospitalization, and to those who had a relevant medical history with the fear of a more serious course in the case of COVID (transplantation patients, patients under chemotherapy, those with a serious

heart disease, etc.). This approach was advocated at the national level during entry into phase 3 of the epidemic, from March 14. This explains why the only patients of our cohort who presented a positive test from mid-March were febrile children under 6 weeks of age and patients with comorbidities.

In addition, the fortuitous discovery in mid-March of a COVID+ 2-month-old infant hospitalized in our departments for the management of biliary atresia, without any infectious, febrile, or respiratory symptoms, made us change the screening policy of children to PCR testing systematically for almost every hospitalization.

At the same time, the capacity of the virology laboratory adapted progressively and multiplied by 20 over a few weeks, thus allowing for more flexibility in the choice of patients to be tested.

The large proportion of asymptomatic patients or patients with mild disease may justify systematic screening in all hospitalized children, more so to protect caregivers and other patients than to prevent secondary complications linked to the virus. The availability of a sufficient number of screening tests and the capacities of hospital laboratories, which has already contributed to the evaluation during the development of the sampling policy, are all parameters to be taken into account when deciding whether or not to extend mass screening to all hospitalizations.

According to our experience, if the principle of testing all patients who must be hospitalized was implemented during non-confinement, it would seem appropriate to organize the samples in private laboratories before scheduled hospitalizations (48 h before), also with a dedicated pediatric screening center located within the hospital for unscheduled admissions and special situations. This would make it possible to pool resources, ensure an optimized sampling

technique and protection for caregivers, and standardize care for hospitals with several pediatric departments.

Confronted with consultations linked to COVID-compatible symptoms, organized screening at the start of the epidemic and systematic testing before hospitalization, the pediatric ED played a central role in developing the patient circuit and carried out nearly 80% of the positive sampling from our series.

Thanks to the experience acquired, it would be licit to entrust the management of the screening facilities to this department. It must, however, be borne in mind that this very time-consuming activity was made possible due to the marked decrease in the department's usual activity. With non-confinement and the plausible rise in the number of daily consultations, it is not unlikely that it will become complicated to reconcile the screening of samples and the continuation of usual activities without a dedicated staff and an adaptation of the premises.

Among the weaknesses of our study, we note its small population (33 patients), and the fact that the 11 additional patients who tested positive, and who could not be included due to the lack of clinical records, represent one quarter of the cohort and their epidemiological and clinical characteristics might have changed our results. However, with the very significant number of adults being tested and admitted during the same period, the SUH was fully affected and the smaller proportion of underage patients could also result from a less severe disease and reduced contagion (perhaps thanks to the early school closures).

## **5. Conclusion**

Children of all ages can be affected by COVID-19. With a high number of clinical presentations and circumstances of diagnosis, but also by a markedly reduced severity, pediatric forms differ greatly from what is observed in adults. In addition, due to the large

proportion of asymptomatic subjects, multiple questions arise concerning the organization of intra-hospital consultation and hospitalization circuits, on the management of care units, and on the indications for screening and its handling in terms of staff and premises. The main difficulty is not treating COVID-19 in children, which most often remains mild, but preventing transmission of the virus to other patients, caregivers, and by extension to the rest of the population.

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### Figures and tables

**Figure 1.** Study flowchart (y = years)

**Figure 2.** Number of tests performed per week (adults and underage patients)

**Table 1.** Epidemiologic characteristics, clinical features, and outcomes of the 33 COVID+ patients under 18 years of age

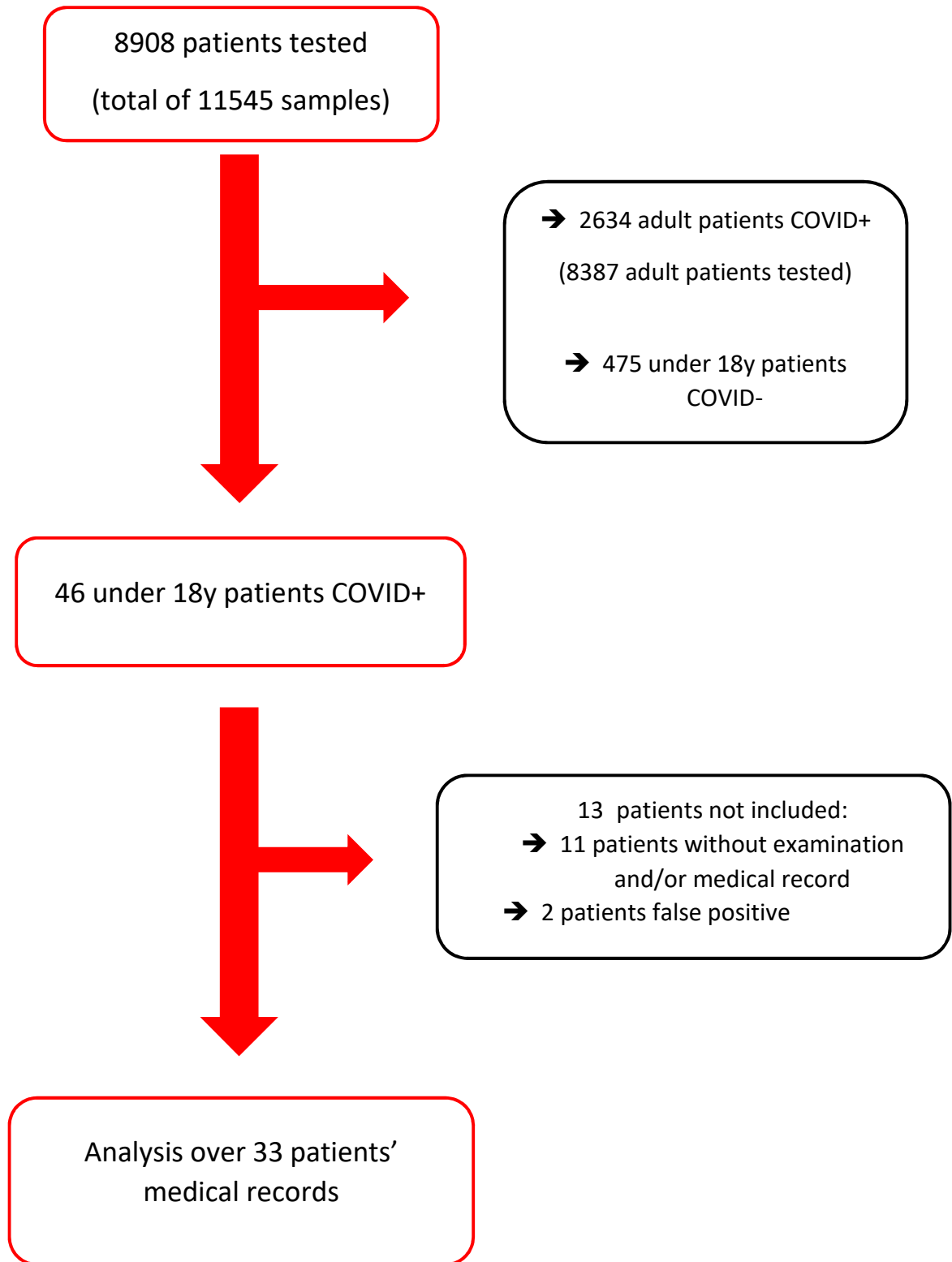
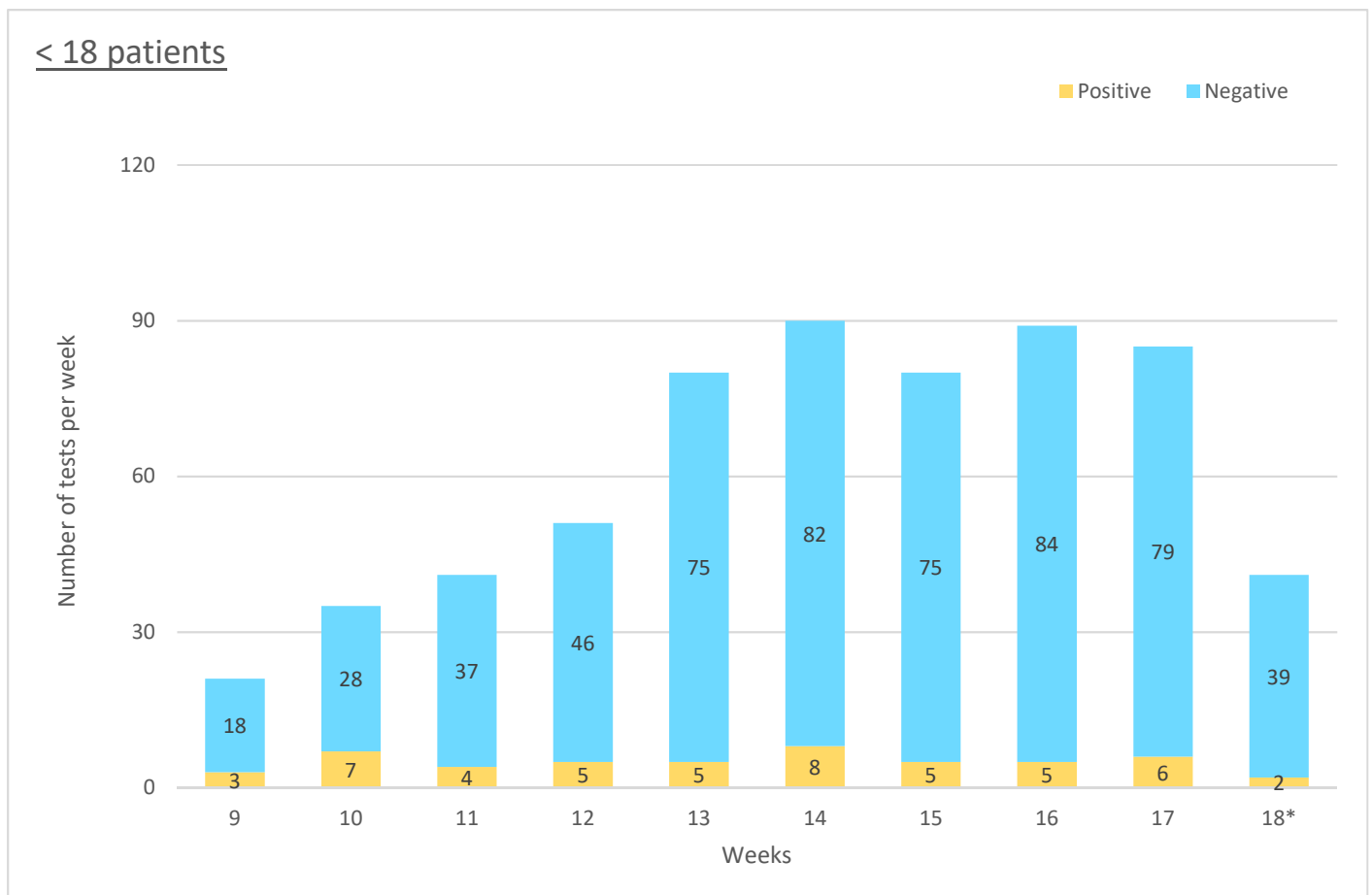
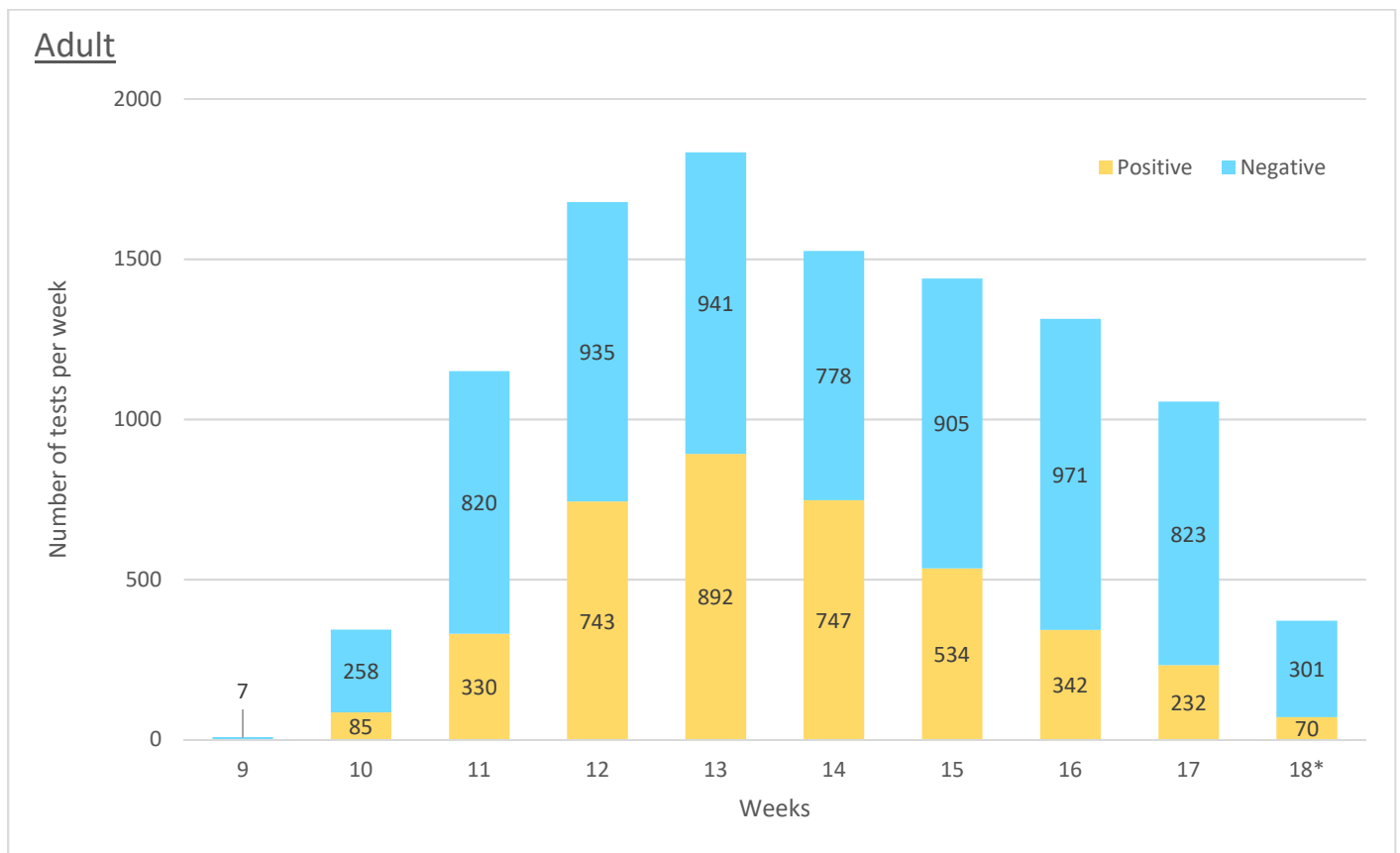


Figure 1. Description of the cohort of the study

Figure 2. Evolution of the number of tests per week



\* Week 18 is not complete and goes from 27/04 to 30/04/20

Table 1. Epidemiologic characteristics, clinical features and outcomes of the 33 under 18y patients COVID+

N = 33

Median age (25% - 75%) – yr	1 year 9 months (1 month – 8 years 9 months)
Mean - yr	5 years and 5 months
Age distribution – no. (%)	
< 1 yr	15 (45.5%)
1–< 6 yr	6 (18.2%)
6–10 yr	4 (12.1%)
> 10 yr	8 (24.2%)
Sex ratio (male/female)	0.6 (19/14)
Coexisting conditions (%)	9 (27.2%)
Symptomatic at time of test (%)	26 (78.8%)
Fever > 38°C (%)	17 (51.6%)
Symptoms (%)*	
Typical presentation : rhinitis and/or cough and/or shortness of breath	18 (54.5%)
Digestive signs (diarrhea, nausea, vomiting, abdominal pain)	6 (18.2%)
Neurological symptoms (headache, agitation and confusion, absence)	3 (9.1%)
General signs (asthenia, myalgia, anorexia, eating difficulties and/or poor weight gain, irritability)	11 (33.3%)
Anosmia and/or ageusia	1 (3%)
Asymptomatic	7 (21.2%)
Unit of realization of the positive tests (%)	
Emergency Departments and Short-Term Hospitalization Unit	26 (78.8%)
Pediatric Surgery	4 (12.2%)
Conventional Pediatric Departments	1 (3%)
Pediatric Onco-hematology	1 (3%)
Neonatology	1 (3%)
Admitted (%)	26 (78.8%)
Resuscitation care (%)	1 (3%)
Diagnosis at discharge (%)	
COVID-19 infection	18 (54.5%)
Linked to a pre-existing pathology	6 (18.2%)
Emergency situations	7 (21.2%)
Died (%)	0

\* The presence of the different types of symptoms is not exclusive for a given patient; yr = years.